CLAIMS

1. A method of screening for a modulator of PLK, wherein the method comprises using the structure co-ordinates of *Table 2*.

2. A method according to claim 1 comprising the steps of:

(a) providing at least a portion of the structure co-ordinates of *Table 2*;

(b) employing at least a portion of the structure co-ordinates of *Table 2* to design or select or synthesise a putative modulator of PLK;

(c) contacting the putative modulator of PLK with PLK or a mutant, variant, homologue, derivative or fragment thereof, in the presence of a substrate of PLK; and

(d) determining whether said putative modulator of PLK modulates PLK.

3. A method according to claim 1 or claim 2 wherein at least a portion of the structure co-ordinates of *Table 2* and/or the putative modulator of PLK and/or the substrate are provided on a machine-readable data storage medium comprising a data storage material encoded with machine readable data.

4. A method according to claim 2 or claim 3 wherein the putative modulator of PLK is selected from a library of compounds.

5. A method according claim 2 or claim 3 wherein the putative modulator of PLK is selected from a database.

6. A method according to claim 2 or claim 3 wherein the putative modulator of PLK is designed *de novo*.

7. A method according to claim 2 or claim 3 wherein the putative modulator of PLK is designed from a known PLK modulator.

8. A method according to claim 2 or claim 3 wherein the design or selection of the putative modulator of PLK is performed in conjunction with computer modelling.

9. A method according to any preceding claim wherein the putative modulator of PLK inhibits PLK activity.

10. A method according to any preceding claim wherein the PLK is PLK1.

11. A method according to any preceding claim wherein the putative modulator of PLK is useful in the prevention and/or treatment of a PLK related disorder.

12. A method according to claim 11 wherein the PLK related disorder is a proliferative disorder.

13. A method according to claim 12 wherein the proliferative disorder is selected from cancer, leukemia, glomerulonephritis, rheumatoid arthritis, psoriasis and chronic obstructive pulmonary disorder.

14. An assay for a candidate compound capable of modulating PLK, said assay comprising the steps of:

(a) contacting said candidate compound with PLK;

(b) detecting whether said candidate compound forms associations with one or more amino acid residues corresponding to PLK amino acid residues L59, G60, A65, C67, A80, K82, L130, E131, C133, R135, F183 and D194.

15. An assay according to claim 14 wherein said candidate compound is selected by performing rational drug design with a 3-dimensional model of PLK in conjunction with computer modelling.

16. An assay according to claim 14 or 15 which comprises detecting whether said candidate compound forms an association with the amino acid residue corresponding to PLK amino acid residue C67.

17. Use of a compound selected from the following:

(i) 5'-thioadenosine, or a derivative thereof;

(ii) staurosporine, wortmannin, purvalanol A, LY294002, quercetin, morin hydrate, or derivatives thereof; and

(iii) 4-[4-(4-methyl-2-methylaminothiazol-5-yl)-pyrimidin-2-ylamino]-phenol; 4-[4-(2,4-dimethyl-thiazol-5-yl)-pyrimidin-2-ylamino]-phenol or 4-[4-(2-amino-4-methyl-thiazol-5-yl)-pyrimidin-2-ylamino]-phenol;

or a pharmaceutically acceptable salt thereof, in an assay for identifying candidate compounds capable of modulating PLK.

18. Use according to claim 17 wherein the assay is a competitive binding assay.

19. Use according to claim 17 or claim 18 wherein the assay comprises contacting a candidate compound with PLK in the presence of a compound selected from:

(i) 5'-thioadenosine, or a derivative thereof;

(ii) staurosporine, wortmannin, purvalanol A, LY294002, quercetin, morin hydrate, or derivatives thereof; and

(iii) 4-[4-(4-methyl-2-methylaminothiazol-5-yl)-pyrimidin-2-ylamino]-phenol, 4-[4-(2,4-dimethyl-thiazol-5-yl)-pyrimidin-2-ylamino]-phenol or 4-[4-(2-amino-4-methyl-thiazol-5-yl)-pyrimidin-2-ylamino]-phenol;

or a pharmaceutically acceptable salt thereof, and detecting any change in the interaction between (i), (ii) or (iii) and PLK.

20. A PLK modulator identified by the method of any one of claims 1 to 13, or a candidate compound identified by an assay according to any one of claims 14 to 19.

21. A PLK modulator or candidate compound according to claim 20 wherein the PLK modulator inhibits PLK activity.

22. A PLK modulator or candidate compound according to claim 20 or claim 21 which is capable of forming a covalent bond with the amino acid residue corresponding to PLK amino acid residue C67.

23. A PLK modulator or candidate compound according to claim 22 which is capable of forming a disulfide bond with the thiol group of the amino acid residue corresponding to PLK amino acid residue C67.

24. A PLK modulator or candidate compound according to claim 20 which is an irreversible antagonist.

25. A pharmaceutical composition comprising a PLK modulator or candidate compound according to any one of claims 20 to 24 and a pharmaceutically acceptable carrier, diluent, excipient or adjuvant or any combination thereof.

26. A method of preventing and/or treating a PLK related disorder comprising administering a PLK modulator or candidate compound according to any one of claims 20 to 24 and/or a pharmaceutical composition according to claim 25 wherein said PLK modulator, said candidate compound or said pharmaceutical, is capable of causing a beneficial preventative and/or therapeutic effect.

27. A method according to claim 26 wherein the PLK modulator or candidate compound is selected from the following:

(i) 5'-thioadenosine, or a derivative thereof:

(ii) staurosporine, wortmannin, purvalanol A, LY294002, quercetin, morin hydrate, or derivatives thereof; and

(iii) 4-[4-(4-methyl-2-methylaminothiazol-5-yl)-pyrimidin-2-ylamino]-phenol, 4-[4-(2,4-dimethyl-thiazol-5-yl)-pyrimidin-2-ylamino]-phenol or 4-[4-(2-amino-4-methyl-thiazol-5-yl)-pyrimidin-2-ylamino]-phenol;

or a pharmaceutically acceptable salt thereof.

28. Use of a PLK modulator according to any one of claims 20 to 24 in the preparation of a medicament for treating a PLK related disorder.

29. A method according to claim 27, or use according to claim 28, wherein the PLK related disorder is cancer.

30. A process comprising the steps of:

(a) performing the method according to any of claims 1 to 13, or an assay according to any one of claims 14 to 19;

(b) identifying one or more modulators of PLK; and

(c) preparing a quantity of said one or more PLK modulators.

31. A process comprising the steps of:

(a) performing the method according to any of claims 1 to 13, or an assay according to any one of claims 14 to 19;

(b) identifying one or more PLK modulators; and

(c) preparing a pharmaceutical composition comprising said one or more identified PLK modulators.

32. A process comprising the steps of:

(a) performing the method according to any of claims 1 to 13, or an assay according to any one of claims 14 to 19;

(b) identifying one or more PLK modulators;

(c) modifying said one or more PLK modulators; and

(d) optionally preparing a pharmaceutical composition comprising said one or more PLK modulators.

33. A computer for producing a three-dimensional representation of PLK wherein said computer comprises:

(a) a computer-readable data storage medium comprising a data storage material encoded with computer-readable data, wherein said data comprises the structure co-ordinates of *Table 2*;

(b) a working memory for storing instructions for processing said computer-readable data;

(c) a central-processing unit coupled to said working memory and to said computer-readable data storage medium for processing said computer-machine readable data into said three-dimensional representation; and

(d) a display coupled to said central-processing unit for displaying said three-dimensional representation.

34. A machine-readable data storage medium comprising a data storage material encoded with machine readable data, wherein the data is defined by at least a portion of the structure co-ordinates of *Table 2*.

35. Use of the computer of claim 33 or the machine readable data storage medium of claim 34 to predict the structure and/or function of potential modulators of PLK.

36. Use of at least a portion of the structure co-ordinates of *Table 2* to screen for modulators of PLK.

37. Use of at least a portion of the structure co-ordinates of *Table 2* to solve the structure of the crystalline form of any other protein with significant amino acid sequence homology to any functional domain of PLK.

38. Use according to claim 37 wherein the structure of the crystalline form of any other protein with significant amino acid sequence homology to any functional domain of PLK is solved using molecular replacement.

39. Use of at least a portion of the structure co-ordinates of *Table 2* in molecular design techniques to design, select and synthesise modulators of PLK.

40. Use of at least a portion of the structure co-ordinates of *Table 2* in the development of compounds that can isomerise to reaction intermediates in the chemical reaction of a substrate or other compound that binds to PLK.

41. Use of at least a portion of the structure co-ordinates of *Table 2* to screen small molecule databases for chemical entities or compounds that modulate PLK.

42. A method of treating a proliferative disorder, said method comprising administering to a subject in need thereof a compound selected from the following:

(i) 5'-thioadenosine, or a derivative thereof;

(ii) staurosporine, wortmannin, purvalanol A, LY294002, quercetin, morin hydrate, or derivatives thereof; and

(iii) 4-[4-(4-methyl-2-methylaminothiazol-5-yl)-pyrimidin-2-ylamino]-phenol, 4-[4-(2,4-dimethylthiazol-5-yl)-pyrimidin-2-ylamino]-phenol or 4-[4-(2-amino-4-methyl thiazol-5-yl)-pyrimidin-2-ylamino]-phenol;

or a pharmaceutically acceptable salt thereof, in an amount sufficient to inhibit PLK such that said proliferative disorder is treated.

43. A method of treating a proliferative disorder comprising inhibiting PLK by administering to a subject in need thereof, a therapeutically effective amount of a compound selected from the following:

(i) 5'-thioadenosine, or a derivative thereof;

(ii) staurosporine, wortmannin, purvalanol A, LY294002, quercetin, morin hydrate, or derivatives thereof; and

(iii) 4-[4-(4-methyl-2-methylaminothiazol-5-yl)-pyrimidin-2-ylamino]-phenol, 4-[4-(2,4-dimethyl-thiazol-5-yl)-pyrimidin-2-ylamino]-phenol or 4-[4-(2-amino-4-methyl-thiazol-5-yl)-pyrimidin-2-ylamino]-phenol;

or a pharmaceutically acceptable salt thereof, such that treatment of the proliferative disorder occurs.

44. A method of treating a PLK dependent disorder in a subject in need thereof, said method comprising administering to said subject a compound selected from the following:

(i) 5'-thioadenosine, or a derivative thereof;

(ii) staurosporine, wortmannin, purvalanol A, LY294002, quercetin, morin hydrate, or derivatives thereof; and

(iii) 4-[4-(4-methyl-2-methylaminothiazol-5-yl)-pyrimidin-2-ylamino]-phenol, 4-[4-(2,4-dimethyl-thiazol-5-yl)-pyrimidin-2-ylamino]-phenol or 4-[4-(2-amino-4-methyl-thiazol-5-yl)-pyrimidin-2-ylamino]-phenol;

or a pharmaceutically acceptable salt thereof, in an amount sufficient to inhibit PLK.

45. A method according to claim 45 wherein the PLK dependent disorder is a disorder associated with increased PLK activity.

46. A method according to claim 44 or claim 45 wherein the disorder is cancer.

47. A method of inhibiting PLK in a cell comprising contacting said cell with an amount of a compound selected from the following:

(i) 5'-thioadenosine, or a derivative thereof;

(ii) staurosporine, wortmannin, purvalanol A, LY294002, quercetin, morin hydrate, or derivatives thereof; and

(iii) 4-[4-(4-methyl-2-methylaminothiazol-5-yl)-pyrimidin-2-ylamino]-phenol, 4-[4-(2,4-dimethyl-thiazol-5-yl)-pyrimidin-2-ylamino]-phenol or 4-[4-(2-amino-4-methyl thiazol-5-yl)-pyrimidin-2-ylamino]-phenol;

or a pharmaceutically acceptable salt thereof, such that PLK is inhibited in said cell.

48. A method according to claim 47 wherein the cell is a cancer cell.

49. A fragment of PLK, or a homologue, mutant, or derivative thereof, comprising a ligand binding domain, said ligand binding domain being defined by the amino acid residue structural coordinates selected from one or more of the following: L59, G60, A65, C67, A80, K82, L130, E131, C133, R135, F183 and D194.

50. A fragment of PLK, or a homologue, mutant or derivative thereof, according to claim 49 which corresponds to a portion of the structure co-ordinates of *Table 2*.

51. Use of a fragment of PLK, or a homologue, mutant, or derivative thereof, according to claim 50 or 51 in an assay for identifying candidate compounds capable of modulating PLK.

52. A method of screening for a modulator of PLK substantially as described herein, and with reference to the accompanying drawings.

53. An assay substantially as described herein, and with reference to the accompanying drawings.

54. A PLK modulator substantially as described herein, and with reference to the accompanying drawings.

55. A process substantially as described herein, and with reference to the accompanying drawings.